

Serial No.: 09/746,036  
Attorney Docket No.: 3363

### **REMARKS**

Applicants have amended Claims 1, 2, 4, 8, 9, 11, 15, 16 and 18. Support for the amendments to Claims 1, 8 and 15 may be found, for example, on page 3 of the Specification; for the amendments to Claims 2, 9 and 16 in the originally filed claims; and for the amendments to Claims 4, 11 and 18 on pages 5 and 19 of the Specification.

Applicants have also amended pages 10-13, 15, and 19 of the Specification to correct typographical errors and to update the status of referenced U.S. applications and attorney docket numbers.

Applicants respectfully request entry of the above amendments and submit that no new matter is presented by these amendments.

#### ***Objections to the Specification are Obviated***

The Examiner has objected to the Disclosure because it contains embedded hyperlinks. Applicants have amended pages 10 and 15 of the Specification to delete the hyperlinks.

Applicants have also updated the status of the multiple listings of Applications by Serial Number or Attorney Docket Number on pages 11-13 and 19 of the Specification.

#### ***Claim Rejections under 35 U.S.C. §101 should be Withdrawn***

The Examiner has rejected Claims 1-7 under 35 U.S.C. §101 because the claimed invention is allegedly directed to non-statutory subject matter.

Specifically, the Office Action alleges that the claims are drawn to methods which manipulate data and do not provide a concrete, tangible and useful result. Applicants

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respectfully disagree with the Examiner, but solely to expedite the issuance of the present Claims, have amended Claim 1 to recite "a computer-implemented method" in the preamble and "analyzing the results of nucleic acid probe array based gene expression experiments for a plurality of transcripts in the plurality of samples using a plurality of nucleic acid probe arrays..." in the body of the claim. Applicants respectfully submit that amended Claim 1 is statutory process indicating manipulation of data representing physical objects (pre-computer process activity) wherein intensities represent hybridization between probes and their targets. In addition, the Claims are limited to a practical application in the technological arts in "analyzing the results of nucleic acid probe array based gene expression experiments for a plurality of transcripts in the plurality of samples using a plurality of nucleic acid probe arrays". Thus the computer-implemented method of Claim 1 produces a concrete, tangible and useful result (*State Street*, 149 F.3d at 1373) and is thereby directed to statutory subject matter.

For the above reasons, Applicants respectfully submit that the rejection of Claims 1-7 under 35 U.S.C. §101 should be withdrawn.

***Claim Rejections under 35 U.S.C. §112 should be Withdrawn***

The Examiner has rejected Claims 1-21 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite.

The Examiner alleges that in independent Claims (1, 8 and 15), it is allegedly unclear what the method of 'analysis' is intended to accomplish. Applicants respectfully disagree with the Examiner, but solely to expedite the issuance of the present Claims, have amended Claims 1, 8 and 15 to recite "analyzing the results of nucleic acid probe

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array based gene expression experiments for a plurality of transcripts in the plurality of samples using a plurality of nucleic acid probe arrays by.....” in the body of the respective Claims. Support for the amendment may be found, for example, on page 3 (lines 20-22) of the Specification.

The Examiner also alleges that it is not clear what the differing result is when one minimizes rather than maximizes. Applicants wish to clarify that the Claims are directed to methods for *minimizing* the effect of cross-hybridization using linear programming. These methods are based on constraining possible expression levels using models (see for example, pages 3 and 4 of the Specification). Some of these models include defining parameters that *maximize* the true effect of hybridization between a probe and a transcript (page 4, lines 9-10). Thus, the terms minimizing and maximizing in the Claims and Specification are consistent rather than being indicative of differing results.

The Examiner has rejected Claims 2, 9 and 16 because the phrase “wherein the minimizing comprising maximizing” is allegedly unclear. Applicants respectfully disagree with the Examiner since the phrase is clear in view of Claims 1, 8 or 15 (respectively), which recite “minimizing the effect of cross-hybridization.” However, solely to expedite the issuance of the Claims, Applicants have amended Claims 2, 9 and 16. Support for the amendment may be found, for example, in the originally filed Claims.

The Examiner has rejected Claims 4, 11 and 18 for allegedly being confusing and grammatically incorrect. Applicants respectfully disagree with the Examiner, but solely to expedite the issuance of the present Claims, have amended Claims 4, 11 and 18. This

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rejection is thus obviated by the amendment. Support for the amendment may be found, for example, on pages 5 (lines 2-4) and 19 (lines 11-14) of the Specification.

Claims 7, 14 and 21 are rejected for allegedly being unclear with respect to the previous methods as well as the results obtained. Applicants respectfully disagree with the Examiner. Claims 7, 14 and 21 are directed to determining confidence intervals for relative transcript levels, couplings and scales by bootstrapping methods. Thus, the Claims are directed to an additional statistical determination (confidence intervals) and are clear to one of skill in the art with respect to the previous methods as well as the results obtained.

In summary, in view of the foregoing arguments and amendments, Applicants respectfully submit that the rejection of Claims 1-21 under 35 U.S.C. §112, second paragraph, should be withdrawn.

***Claim Rejections under 35 U.S.C. §102 should be Withdrawn***

Claims 1, 8 and 15 are rejected under 35 U.S.C. §102(e) for allegedly being anticipated by Balaban (US Patent No. 6,510,391).

Applicants respectfully disagree with the Office Action. Balaban teaches methods for determining hybridization between a probe and its target which include adjusting hybridization intensities of each probe by dividing the intensities by the probe affinities and using a minimal adjusted hybridization intensity as a measure of gene expression. Balaban does not disclose the use of linear programming to minimize the effect of cross-hybridization in the analysis of nucleic acid probe array-based gene expression data.

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In summary, since the cited reference fails to disclose each and every element of the claimed invention, Applicants respectfully submit that the rejection of Claims 1, 8 and 15 under 35 U.S.C. § 102(e) should be withdrawn.

### CONCLUSION

For these reasons, Applicants believe the application is now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,



Priyadarshini Rath

Limited Recognition under 37 CFR 10.9(b)

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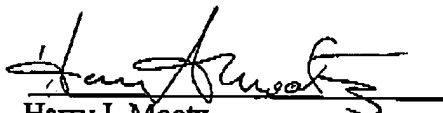
**BEFORE THE OFFICE OF ENROLLMENT AND DISCIPLINE  
UNITED STATE PATENT AND TRADEMARK OFFICE**

**LIMITED RECOGNITION UNDER 37 CFR § 10.9(b)**

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**Expires: July 5, 2004**



Harry I. Moatz

Director of Enrollment and Discipline